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10/807,897	03/24/2004	Rong Xiang	TSRI 874.1	6550

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EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/807,897	XIANG ET AL.	
	Examiner	Art Unit	
	WU-CHENG Winston SHEN	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,26,28 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 26, 28, and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim amendments filed on 07/17/2008 have been entered. Claims 2-25, 27, and 29-52 are cancelled. Claim 1 has been amended. Claims 1, 26, 28, and 53 are pending and currently.

This application 10/807,897 filed on March 24, 2004 claims the benefit of 60/457,009 filed on 03/24/2003.

Claim Rejection - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Previous new matter rejection of claims 1, 26, 28, and 53 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is ***withdrawn*** because the claims have been amended.

The amended independent claim 1 file don 07/17/2008 no longer recites the limitation "at least one CCL21 cytokine". Claims 26, 28, and 53 depend from claim 1.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claim 1 remains rejected under 35 U.S.C. 103(a) as being unpatentable over **Rovero et al.** (Rovero et al. Insertion of the DNA for the 163-171 peptide of IL1beta enables a DNA vaccine encoding p185 (neu) to inhibit mammary carcinogenesis in Her-2/neu transgenic BALB/c mice. *Gene Ther.* 8(6): 447-52, 2001) in view of **Gordan et al.** (Gordan et al. Universal tumor antigens as targets for immunotherapy, *Cytotherapy*, 4(4):317-27, 2002), **Nagira et al.** (Nagira et al., A lymphocyte-specific CC chemokine, secondary lymphoid tissue chemokine (SLC), is a highly efficient chemoattractant for B cells and activated T cells. *Eur J Immunol.* 28(5):1516-23, 1998), and **Lu et al.** (US 5,733,760, issued 03/31/1998). Applicant's arguments filed 07/17/2008 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 7-13 of the office action mailed on 04/25/2008.

Applicant's arguments and Response to Applicant's arguments

(i) Applicant argues that, in essence, the Office Action asserts that the *de novo* rebuilding of the Rovero vaccine utilizing survivin DNA and CCL21 DNA in an attenuated *Salmonella typhimurium* vector would have been obvious due to the reported biological properties of the various components. Applicant argues that this argument is nothing more than a variant on the "obvious to try" standard, in which the person of ordinary skill in the art is expected to vary all parameters or to try each of numerous possible choices until one possibly arrived at a successful

result. Applicant states that The Supreme Court has indicated that "obvious to try" may amount to "obvious" when there "are a finite number of identified, predictable solutions, [and] a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." See KSR Int'l Co. v. Teleflex Inc. 127 S. Ct. 1727 (2007). That is not the case here, however. (See second paragraph, page 4, Applicant's reply filed on 07/17/2008).

In response: Applicant's arguments have been fully considered and found not persuasive. It is noted that the following statements have been clearly documented on pages 11-12 of the office mailed on 04/25/2008.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to generate a DNA vaccine construct to be incorporated into and delivered by *Salmonella* vector, as taught by Lu et al (1998), via modification of the DNA vaccination construct to encode survivin as an universal tumor associated antigen, as taught by Gordan et al., and CCL21 as a cytokine, as taught by Nagira et al., 1997. It would have been obvious to replace the breast tumor specific antigen Her-2/neu ($p185^{neu}$) with non-breast cancer restricted universal tumor associated antigen survivin, taught by Gordan et al., and replace the DNA encoding cytokine IL-1β peptide taught by Rovero with DNA encoding cytokine CCL21, as taught by Nagira et al. Such a DNA construct encoding both survivin and CCL21, would elicit an immune response against various cancer cells via both activation of B cell mediated production of antibody against survivin, which is universally expressed in all tumor cells, and T cell mediated cytolytic response enhanced by cytokine CCL21-directed immune response in a tumor cell specific manner.

One having ordinary skill in the art would have been motivated to replace the breast tumor specific antigen Her-2/neu ($p185^{neu}$) with non-breast cancer restricted tumor specific antigen survivin, taught by Gordan et al., and replace DNA encoding cytokine IL-1β peptide with DNA encodes cytokine CCL21/SLC, as taught by Nagira et al., and incorporating the DNA construct into a *Salmonella* vector because (i) survivin is universally expressed in all human tumors, and the features of universal TAA indicate a pre-existing, high-affinity T-cell pool that can be activated *in vivo* in patients, without immunoselection of variant tumor cells no longer expressing the Ag of choice, (ii) CCL21/SLC can enhance immune response against tumor specific antigen via both activation of T cells and attraction of B cells that produce antibody against survivin, which is universally expressed in all human tumor cells, and T cell mediated cytolytic response and B cell mediated immune response enhanced by cytokine CCL21 directed immune response in a tumor cell specific manner, (iii) attenuated *Salmonella typhimurium* provides effective delivery of desired antigens by oral vaccination as large scale production of attenuated *Salmonella* vectors can facilitate the vaccination process and effectiveness.

Based on the reasons stated above, the Examiner maintains the position that the rejection is based on clear teachings, suggestion, and motivation collectively disclosed by the cited references, not just an random unjustified "obvious to try". The Examiner agrees with the Applicant with regard to the statements that The Supreme Court has indicated that "obvious to try" may amount to "obvious" when there "are a finite number of identified, predictable solutions, [and] a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." See KSR Int'l Co. v. Teleflex Inc. 127 S. Ct. 1727 (2007). Even if the rejection were to be considered under "obvious to try", it is worth noting the status of art

indicates that there is a finite number of TAA (tumor associated antigen) universally expressed in all human tumors, including survivin (which is in contrast to the breast tumor specific antigen Her-2/neu), and the universally expressed TAA such as survivin features a pre-existing, high-affinity T-cell pool that can be activated *in vivo* in patients, without immunoselection of variant tumor cells no longer expressing the Ag of choice. Similarly, the status of art indicates that there is a finite number of cytokines, such as CCL21 (which is in contrast to cytokine IL-10 that fails to affect the effectiveness of the immunization, see page 6 of the Final office action mailed on 07/06/2007), which has been demonstrated to enhance immune response against tumor associated antigen via both activation of T cells and attraction of B cells that produce antibody against the tumor associated antigen, e.g. the universally expressed TAA, survivin. Therefore, it is certainly "obvious to try" to have a DNA vaccine suitable for eliciting an immune response against any cancer cells comprising a DNA construct that expresses a survivin protein and a CCL21 cytokine, as encompassed by the claimed invention.

(ii) Applicant argues that the present invention does not represent a *predictable* variation of known elements or techniques in prior arts or fields of endeavor. Applicant indicates that, in the previous Office Action, which rejected the original claims for lack of enablement, the anti-cancer art is relatively unpredictable. Applicant argues that the DNA vaccines of the present invention can be characterized as a novel form of "gene therapy" in that the vaccine must transfect antigen presenting cells (APC) in order to elicit an immune response, and this is also a very unpredictable field. Applicant argues that, the present rejection simply presupposes, without any basis in fact, too much knowledge and predictability on the part of the person of

ordinary skill and the field of endeavor, in a manner which is wholly inconsistent with the Examiner's prior position *vis-a-vis* the alleged lack of enablement of the prior claims, in which the unpredictability of the art was asserted. Applicant argues that in the present case, there are many potential choices for the tumor antigen and for the selection of a cytokine adjuvant, coupled with the need to select a delivery vehicle that will be effective for both the tumor antigen and the cytokine. The selection of all of these variants based on the applied art would clearly have involved undue experimentation (See third paragraph, page 4, Applicant's reply filed on 07/17/2008).

In response: As documented on pages 2-3 of the Non-Final office action mailed on 04/25/2008, previous rejection of claims 1, 26-29, and 53 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA vaccine suitable for eliciting an immune response against cancer cells comprising a DNA construct operably encoding at least one survivin protein and at least one CCL21 cytokine in a pharmaceutically acceptable carrier, does not reasonably provide enablement for the said method comprising *any cytokine*, has been ***withdrawn*** because the claims had been amended to recited cytokine CCL21, which has been determined to be the enabled scope of the claimed invention (See pages 2-3 of the Non-Final office action mailed on 04/25/2008). It is worth noting that as documented on pages 4-6 of the Final office action mailed on 07/06/2007, the withdrawn scope of enablement is focused on the unpredictability of any cytokine to enhance the effectiveness of a DNA vaccine, for instance IL-10 fail to affect the effectiveness of the immunization (See page 6 of the Final office action mailed on 07/06/2007). Therefore, there is no inconsistency of Examiner position pertaining to the predictability of elicitation of an immune response in a subject upon administration of a DNA

vaccine (or a DNA molecule expressing a foreign protein in general) to the subject and, in contrast, the unpredictability of any cytokine in affecting effectiveness of a DNA vaccine. Furthermore, a scope of enablement rejection, in this case already withdrawn, does not in any way preclude a rejection under 35 U.S.C. 103(a) which is directing to the scoped enabled embodiments encompassed by the claimed invention.

(iii) Applicant argues that the principal reference, Rovero et al., discloses a plasmid DNA vaccine (not a bacterial vector) encoding the tumor antigen Her-2/neu (not survivin) and an immunologically active fragment of IL-1β (not CCL21), and the reference reports that immunization with this vaccine elicited lymphocyte infiltration into the stroma surrounding the terminal ductal-lobular units (TDLU) and induction of antibodies against the Her-2/neu antigen (anti- p185neu), and delayed tumor appearance in mice, but did not induce significant cytotoxic T lymphocyte (CTL) response (see page 449, col. 2, last full paragraph). Applicant argues that in contrast, the presently claimed vaccine does indeed elicit activation of CTLs (i.e., CD8 T cells), and the present application indicates that while a vaccine encoding only the survivin protein did induce some anti-tumor response, the claimed combination encoding both survivin and CCL21 was significantly more effective (see in particular the results described in Examples 4, 5, and 17, on pages 33-35 and 44-45, demonstrating significant CD8 T cell activation in mice treated with the claimed vaccines, and Examples 3, 8, and 15, on pages 31- 33, 36-37, and 41-43). (See page 5, Applicant's reply filed on 07/17/2008). Accordingly, Applicant asserts that the present invention provides benefits and results that are unexpected and could not have been predicted based on the teachings of the prior art. Applicant indicates that, for example, the data

in Table 2, on page 35, clearly demonstrate a significant upregulation of CD8 T-cells that express CD25, CD28 and CD69 activation markers, in comparison to examples involving only the survivin protein or only the CCL21. These increased expression levels would not have been predictable from the allied prior art, i.e., Nagira et al., which does not disclose or even suggest the enhanced expression of these T-cell markers by CCL21 (See bridging paragraph, pages 6-7, Applicant's reply filed on 07/17/2008).

In response: It is noted that the induction of cytotoxic T lymphocyte (CTL) response by the claimed DNA vaccine is not recited in the amended claim filed on 07/18/2008. The claims with recitation of "an immune response against cancer cells" as written encompasses any immune response directly or indirectly against cancer cells, which certainly read on the immune response caused by a plasmid DNA vaccine taught by Rovero et al.

The Examiner acknowledges that Rovero et al. does not teach using bacterial vector (i.e. *Salmonella typhimurium* recited in claim 1), therefore, Rovero does not anticipate the claimed invention, but makes it obvious in combination with the cited art of record. It has been clearly documented in the 103 rejection that the advantages of a vaccine comprising attenuated *Salmonella typhimurium* as a vector to express exogenous antigen(s) that can be delivered orally for vaccination and targets Peyer's patches in the gut, are known in the art. In this regard, **Lu et al.** (1998) teaches the following: Attenuated *Salmonella typhimurium* has been proposed as one means of providing effective delivery of desired antigens. They provide the advantage that they can be delivered orally. The bacteria grow rapidly and do not require growth in cell culture. Thus, large scale production of vectors, for example, in the use of vaccines, can be accomplished more quickly and easily than where mammalian tissue cultures are required. After oral

ingestion, *Salmonella* are concentrated within the liver, spleen, bone marrow, and the Peyers' patches of the gut-associated lymphoid tissue (GALT) (See Abstract, and lines 39-54, column 1, Lu et al., 1998).

Applicant's arguments pertaining to the claimed DNA vaccine presenting unexpected results have been fully considered and found not persuasive. The following statements have been documented on pages 12-13 of the office action mailed on 04/25/2008: There would have been a reasonable expectation of success given (i) successful DNA vaccine construct encodes both Her2 and IL-1β in eliciting immune responses to breast cancer specific tumor antigen Her2 by the teachings of Rovero et al., and (ii) successful identification and validation of survivin as an universal tumor associated antigen as a target of cancer immunotherapy, by the teachings of Gordan et al., (iii) successful demonstration of the effect of CCL21 in increasing T cell mediated cytolytic response as well as B cell recruitment, by the teachings of Nagira et al., and (iv) successful generation of attenuated *Salmonella typhimurium* that can express exogenous antigens and the demonstration of using attenuated *Salmonella typhimurium* for oral vaccination, by the teachings of Lu et al., 1998.

Collectively as discussed above in the section under Applicant's arguments and Response to Applicant's arguments, previous rejection is maintained for the reasons of record advanced on pages 7-13 of the office action mailed on 04/25/2008.

3. Claim 26 remains rejected under 35 U.S.C. 103(a) as being unpatentable over **Rovero et al.** (Rovero et al. Insertion of the DNA for the 163-171 peptide of IL1beta enables a DNA vaccine encoding p185 (neu) to inhibit mammary carcinogenesis in Her-2/neu transgenic

BALB/c mice. *Gene Ther.* 8(6): 447-52, 2001) in view of **Gordan et al.** (Gordan et al. Universal tumor antigens as targets for immunotherapy, *Cytotherapy*, 4(4):317-27, 2002), **Nagira et al.** (Nigira et al., A lymphocyte-specific CC chemokine, secondary lymphoid tissue chemokine (SLC), is a highly efficient chemoattractant for B cells and activated T cells. *Eur J Immunol.* 28(5):1516-23, 1998), **Lu et al.** (US 5,733,760, issued 03/31/1998) as applied to claim 1 above, and further in view of **Bennett et al.** (Bennett et al. WO200157059-A1 and U.S. Patent No. 6,335,194, SEQ ID No: 10, columns 27, 53-55; this reference has been provided in the Non-Final office action mailed on 12/13/2006). Applicant's arguments filed 07/17/2008 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 13-17 of the office action mailed on 04/25/2008.

Applicant's arguments and Response to Applicant's arguments are the same as discussed in the maintained rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Rovero et al. (2001) in view of Gordan et al. (2002), Nagira et al. (1998), and Lu et al. (1998). The distinction of the instant rejection of claim 26 is that **Bennett et al.** teach DNA encoding mouse survivin that identical to SEQ ID NO: 3.

4. Claim 28 remains rejected under 35 U.S.C. 103(a) as being unpatentable over **Rovero et al.** (Rovero et al. Insertion of the DNA for the 163-171 peptide of IL1beta enables a DNA vaccine encoding p185 (neu) to inhibit mammary carcinogenesis in Her-2/neu transgenic BALB/c mice. *Gene Ther.* 8(6): 447-52, 2001) in view of **Gordan et al.** (Gordan et al. Universal tumor antigens as targets for immunotherapy, *Cytotherapy*, 4(4):317-27, 2002), **Nagira et al.** (Nigira et al., A lymphocyte-specific CC chemokine, secondary lymphoid tissue

chemokine (SLC), is a highly efficient chemoattractant for B cells and activated T cells. *Eur J Immunol.* 28(5):1516-23, 1998), **Lu et al.** (US 5,733,760, issued 03/31/1998) as applied to claim 1 above, and further in view of **Tanabe et al.** (Tanabe et al., direct submission, submitted to Genetics Institute, 87 Cambridge Park Drive, Cambridge, MA 02140, USA, on 03-JUN-1997, direct submission of DNA sequences of CCL21; this reference has been provided in the Non-Final office action mailed on 12/13/2006). Applicant's arguments filed 07/17/2008 have been fully considered and they are not persuasive. Previous rejection is ***maintained*** for the reasons of record advanced on pages 17-21 of the office action mailed on 04/25/2008.

Applicant's arguments and Response to Applicant's arguments are the same as discussed in the maintained rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Rovero et al. (2001) in view of Gordan et al. (2002), Nagira et al. (1998), and Lu et al. (1998). The distinction of the instant rejection of claim 28 is that **Tanabe et al.** teach DNA encoding mouse CCL21 that is identical SEQ ID NO: 7 disclosed in instant application.

5. Claim 53 remains rejected under 35 U.S.C. 103(a) as being unpatentable over **Rovero et al.** (Rovero et al. Insertion of the DNA for the 163-171 peptide of IL1beta enables a DNA vaccine encoding p185 (neu) to inhibit mammary carcinogenesis in Her-2/neu transgenic BALB/c mice. *Gene Ther.* 8(6): 447-52, 2001) in view of **Gordan et al.** (Gordan et al. Universal tumor antigens as targets for immunotherapy, *Cytotherapy*, 4(4):317-27, 2002), **Nagira et al.** (Nigira et al., A lymphocyte-specific CC chemokine, secondary lymphoid tissue chemokine (SLC), is a highly efficient chemoattractant for B cells and activated T cells. *Eur J Immunol.* 28(5):1516-23, 1998), **Lu et al.** (US 5,733,760, issued 03/31/1998) as applied to claim

1 above, and further in view of **Bennett et al.** (Bennett et al. WO200157059-A1 and U.S. Patent No. 6,335,194, SEQ ID No: 10, columns 27, 53-55; this reference has been provided in the Non-Final office action mailed on 12/13/2006), and **Tanabe et al.** (Tanabe et al., direct submission, submitted to Genetics Institute, 87 Cambridge Park Drive, Cambridge, MA 02140, USA, on 03-JUN-1997, direct submission of DNA sequences of CCL21; this reference has been provided in the Non-Final office action mailed on 12/13/2006). Previous rejection is ***maintained*** for the reasons of record advanced on pages 21-24 of the office action mailed on 04/25/2008.

Applicant's arguments and Response to Applicant's arguments are the same as discussed in the maintained rejection of claim 1 under 35 U.S.C. 103(a) as being unpatentable over Rovero et al. (2001) in view of Gordan et al. (2002), Nagira et al. (1998), and Lu et al. (1998). The distinction of the instant rejection of claim 28 is that **Bennett et al.** teach DNA encoding mouse survivin that identical to SEQ ID NO: 3, and Tanabe et al. teach DNA encoding mouse CCL21 that is identical SEQ ID NO: 7 disclosed in instant application.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR

1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. No claim is allowed.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you

would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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